

Appl. No. 10/006,881
Amdt. dated September 13, 2004
Amendment under 37 CFR 1.116 Expedited Procedure
Examining Group

PATENT**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (currently amended): A method for production of virus or viral antigen, comprising the steps of (a) providing a culture of adherent cells bound to a microcarrier; (b) growing the cell culture to confluence; (c) infecting the cells with a virus; (d) incubating said culture cells infected with said virus to propagate said virus, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell density is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b); and (e) harvesting the virus or viral antigen produced.

Claim 2 (previously presented): The method according to claim 1, wherein the density of the cell culture grown to confluence is increased at least about 1.3 fold.

Claim 3 (previously presented): The method according to claim 1, wherein the cell density of the cell culture grown to confluence is between about 0.6×10^6 and about 7.0×10^6 cells/ml.

Claim 4 (previously presented): The method according to claim 1, wherein the microcarrier is selected from the group consisting of microcarriers made of dextran, collagen, polystyrene, polyacrylamide, gelatine, glass, cellulose, polyethylene and plastic.

Claim 5 (previously presented): The method according to claim 1, wherein the microcarrier concentration in the culture of cells of step (a) is between about 0.5 g/l and about 14 g/l.

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Claim 6 (previously presented): The method according to claim 1, wherein said cells are selected from the group consisting of adherent cells of VERO, BHK, CHO, RK, RK4, RK13, MRC-5, MDCK, CEF and diploid monolayer cells.

Claim 7 (previously presented): The method according to claim 1, wherein said cells bound to a microcarrier are grown in serum free medium.

Claim 8 (previously presented): The method according to claim 1, wherein said cells bound to a microcarrier are grown in serum and protein free medium.

Claim 9 (previously presented): The method according to claim 1, wherein the virus is selected from the group consisting of Influenza virus, Ross River Virus, Hepatitis A Virus, Vaccinia Virus and recombinant derivatives thereof, Herpes Simplex Virus, Japanese encephalitis Virus, West Nile Virus, Yellow Fever Virus and chimeras thereof, Rhinovirus and Reovirus.

Claim 10 (canceled).

Claim 11 (currently amended): A method for production of purified virus or virus antigen comprising the steps of:

- (a) providing a culture of adherent cells bound to a microcarrier;
- (b) growing the cell culture to confluence;
- (c) infecting the culture of cells with a virus;
- (d) incubating said culture of cells infected with said virus to propagate said virus;
- (e) harvesting the virus produced; and
- (f) purifying said virus harvested, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell culture is

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maintained at ~~high~~ the increased cell density during step (d) as compared to the biomass grown to confluence during step (b).

Claim 12 (previously presented): The method according to claim 11, wherein the virus produced is harvested from the cell culture supernatant.

Claim 13 (previously presented): The method according to claim 11, wherein the virus produced is harvested from the cell biomass.

Claim 14 (currently amended): A method for production of Influenza virus, comprising the steps of:

- (a) providing a culture of adherent cells bound to a microcarrier;
- (b) growing the cell culture to confluence;
- (c) infecting the cells with an Influenza virus;
- (d) incubating said culture of cells infected with said Influenza virus to propagate said virus, wherein the cell density of the biomass of the cell culture grown to confluence is increased by reduction of working volume (i) prior to step (c) or (ii) after step (c) while the cells are bound to said microcarrier, and wherein the cell culture is maintained at the increased cell density during step (d) as compared to the biomass grown to confluence during step (b); and
- (e) harvesting said Influenza virus or Influenza virus antigen produced

Claim 15 (previously presented): The method according to claim 14, wherein said cells are VERO cells.

Claim 16 (previously presented): The method according to claim 14, wherein said cells are MDCK cells.

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Claim 17 (previously presented): The method according to claim 14, wherein said cells bound to a microcarrier are grown in serum free medium.

Claim 18 (previously presented): The method according to claim 14, wherein said cells bound to a microcarrier are grown in serum and protein free medium.

Claim 19 (previously presented): The method according to claim 14, wherein the cell culture grown to confluence is concentrated increased at least about 1.3 fold.

Claim 20 (canceled).

Claim 21 (previously presented): The method according to claim 14, further comprising the step (f) of purifying said Influenza virus harvested.

Claims 22-38 (canceled).

Claim 39 (previously presented): The method according to claim 1, wherein the cell culture in step (d) is maintained for at least three days.

Claim 40 (new): The method according to claim 9, wherein the virus is Influenza virus.

Claim 41 (new): The method according to claim 9, wherein the virus is Ross River Virus.

Claim 42 (new): The method according to claim 9, wherein the virus is selected from the group consisting of Vaccinia Virus and recombinant derivatives thereof.

Claim 43 (new): The method according to claim 9, wherein the virus is Japanese encephalitis Virus, West Nile Virus, Yellow Fever Virus and chimeras thereof.